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EXAMINER	
LEUNG, JENNIFER A	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)
	10/626,436	JENSEN ET AL.
	Examiner	Art Unit
	Jennifer A. Leung	1797

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,4,7-14,16-30,33-37 and 116-119* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,4,7-14,16-30,33-37 and 116-119* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Jennifer A. Leung

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5) ☐ Notice of Informal Patent Application

6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's amendment filed on October 12, 2007 has been considered. Claims 1, 2, 5, 6, 15, 31, 32 and 38-115 are canceled. Claims 3, 4, 7-14, 16-30, 33-37 and 116-119 are active.

Claim Objections

2. Claims 11-13 are objected to because of the following informalities:

The means for introducing a first, second or third reactant into said microreactor at a first, second or third inlet channel is defined in Applicant's specification as inlet port (e.g., at **14**, **18**, **20**; see FIG. 1A and page 12, lines 23-24). Thus, the relationship between the "means" and the "at least one inlet port" now set forth in claim 116, line 6, is rendered unclear.

Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 4, 7-12, 14, 16-30, 116 and 117 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al. (*Chem. Commun.* 2002, pp. 1462-1463) in view of Yasuda et al. (US 6,244,738).

Regarding claims 116, 4, 7-10 and 21, Wang et al. (see entire publication) discloses an apparatus comprising:

at least one inlet channel (i.e., the two channels forming the Y-shape inlet, FIG. 1);

at least one inlet port into the at least one inlet channel (i.e., the openings to the two channels forming the Y-shaped inlet, FIG. 1);

at least one micromixing block (i.e., at the intersection of the two channels formed by the Y-shaped inlet, FIG. 1) positioned downstream from the at least one inlet channel;

an aging section (i.e., the serpentine channel portion, downstream of the Y-shaped inlet; FIG. 1) positioned downstream from the at least one micromixing block; and

at least one outlet channel (i.e., at the Y-shaped outlet, to **3**; FIG. 1) positioned downstream from the aging section;

wherein the inlet channel, micromixing block, aging section and outlet channel reside on one integrated substrate (i.e., a ceramic substrate).

The recitation of "at least one colloidal nanoparticle" adds no further patentable weight because the inclusion of a material or article worked upon by an apparatus does not further limit apparatus claims. In any event, Wang et al. further discloses that the apparatus may be used for synthesizing colloidal nanoparticles (e.g., titania particle having a size of less than 10 nm).

Wang et al. further discloses that the depth, width and length of the aging channel are within the instantly claimed ranges (i.e., a channel depth of 200 μm, a channel width of 360 μm,

and a channel length of 9 cm; at page 1462, column 1, second to last paragraph). Wang et al., however, does not specify the width and depth measurement for the at least one inlet channel or the channel of the micromixing block. In any event, it would have been obvious for one of ordinary skill in the art at the time the invention was made to select an appropriate width and depth (such as a width and depth within the instantly claimed ranges) for the various channels in the apparatus of Wang et al., on the basis of suitability for the intended use and absent showing any unexpected results thereof, because it has been held that changes in size involve only ordinary skill in the art. *In re Rose*, 220 F.2d 459, 463, 105 USPQ 237, 240 (CCPA 1955), and where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art, *In re Aller, 105 USPQ 233*.

In addition, Wang et al. is silent as to the apparatus comprising an ultrasonication means. Yasuda et al., however, teaches an apparatus comprising a microchannel **20**, wherein the apparatus further comprises an ultrasonication means for mixing, in the form of an ultrasonication transducer attached to the apparatus (see elements **31**, **32**, **33**, **41**, **42**, **43**; FIG. 1, 2; column 1, line 5 to column 3, line 36). It would have been obvious for one of ordinary skill in the art at the time the invention was made to provide an ultrasonication means in the apparatus of Wang et al., on the basis of suitability for the intended use, because the ultrasonication means comprises a stirrer having a structure that does not cause an increase in flow resistance in the channel, and is not susceptible to drops remaining in the channel, as taught by Yasuda et al. (column 1, lines 50-54).

Regarding claims 11 and 12, Wang et al. further discloses that the apparatus comprises means for introducing a first reactant stream and a second reactant stream into a first inlet

channel and a second inlet channel, respectively (i.e., via syringe and pumps at **1**; see FIG. 1). As defined in Applicant's specification, the means for introducing a reactant comprises an inlet port (e.g., at **14, 18, 20**; FIG. 1A; page 12, lines 23-24).

Regarding claim 14, the modified apparatus of Wang et al. structurally meets the claims, because the particular number of reactants to be fed to a single inlet channel is considered a process or intended use limitation that adds no further patentable weight to the apparatus claim. Each inlet channel is structurally capable of conveying more than one reactant.

Regarding claims 16-18 and 117, the modified apparatus of Wang et al. structurally meets the claims because the first and second reactant streams are not considered elements of the apparatus, and their respective flow rates are considered process limitations.

Regarding claims 19, 20 and 22-30, the modified apparatus of Wang et al. structurally meets the claims because the synthesized nanoparticles (i.e., the products) are not considered elements of the apparatus.

4. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al. (*Chem. Commun.* 2002, pp. 1462-1463) in view of Yasuda et al. (US 6,244,738), as applied to claim 116 above, and further in view of Chandler et al. (US 6,506,584).

The collective teaching of Wang et al. and Yasuda et al. is silent as to whether the ultrasonication means may comprise an ultrasonication bath, in which the microreactor or a portion thereof is emersed. Chandler et al. (column 5, lines 4-26; column 7, line 24 to column 8, line 18; FIGs. 2, 4) teaches a conventionally known ultrasonication means comprising an ultrasonication transducer or an ultrasonication bath. It would have been obvious for one of ordinary skill in the art at the time the invention was made to substitute the ultrasonication means

of Chandler et al. for the ultrasonication means in the modified apparatus of Wang et al., on the basis of suitability for the intended use thereof and absent showing any unexpected results thereof, because the substitution of known equivalent structures involves only ordinary skill in the art. *In re Fout* 213 USPQ 532 (CCPA 1982); *In re Susi* 169 USPQ 423 (CCPA 1971); *In re Siebentritt* 152 USPQ 618 (CCPA 1967); *In re Ruff* 118 USPQ 343 (CCPA 1958).

5. Claims 13, 33-37, 118 and 119 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al. (*Chem. Commun.* 2002, pp. 1462-1463) in view of Yasuda et al. (US 6,244,738), as applied to claims 11, 12 and 116 above, and further in view of Barbera-Guillem et al. (US 6,179,912).

Regarding claims 13 and 118, Wang et al. is silent as to a means for introducing a third reactant stream into the microreactor at a third inlet channel. In any event, it would have been an obvious design choice for one of ordinary skill in the art at the time the invention was made to add another inlet channel to the apparatus of Wang et al., on the basis of suitability for the intended use and absent a showing of unexpected results thereof, because the duplication of parts was held to have been obvious. *St. Regis Paper Co. v. Beemis Co. Inc.* 193 USPQ 8, 11 (1977); *In re Harza* 124 USPQ 378 (CCPA 1960). For instance, Barbera-Guillem et al. evidences that it would have been obvious for one of ordinary skill in the art at the time the invention was made to add a third inlet channel to an apparatus for synthesizing nanoparticles, in order to allow for three separate reagents or solvents **A**, **B**, **C** to be fed to the microreactor, for synthesizing a particular nanoparticle composition (see FIG. 1). The recitation with respect to the flow rate of a third reactant stream, however, has not been given patentable weight, because the recitation is considered a process limitation.

Regarding claims 33-37 and 119, Wang et al. is silent as to the apparatus comprising a quench fluid inlet port downstream from the aging section and upstream from the at least one outlet channel. Barbara-Guillem et al., however, teaches that, "As is known to those skilled in the art, and depending on the nature of the desired semiconductor nanocrystals produced, growth termination may be achieved by one or more processes which include, but are not limited to, reducing the temperature of the sol containing the semiconductor nanocrystals to a temperature effective for halting further crystalline growth (e.g., a cooling process); and the addition of a crystal growth terminator, to the sol containing the semiconductor nanocrystals, in an effective amount for halting further crystalline growth after a desired size is obtained." (see column 13, lines 50-62; also, generally, column 13, line 50 to column 14, line 49). It would have been obvious for one of ordinary skill in the art at the time the invention was made to further provide a quench fluid inlet port downstream from the aging section and upstream from the at least one outlet channel in the modified apparatus of Wang et al., on the basis of suitability for the intended use, because a quench fluid inlet port would allow for the introduction of a quench fluid (e.g., a growth terminator), for halting further crystalline growth, as is conventional in the art of nanocrystal synthesis, as taught by Barbara-Guillem et al. The recitations with respect to a particular quench fluid, however, have not been given patentable weight, because the quench fluid is not considered part of the apparatus.

6. Claims 4, 7-14, 16-30, 33-37 and 116-119 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan et al. (*Nano Letters*, 2003, Vol. 3, No. 2, pp. 199-201) in view of Yasuda et al. (US 6,244,738).

Regarding claims 116, 4 and 7-10, Chan et al. discloses an apparatus (see FIG. 1 and its

description on page 200; also, generally, see entire publication) comprising:

at least one inlet channel (i.e., the channels immediately communicating with the "Inject" and "Dilute" vias; see flow direction in **b**);

at least one inlet port into the at least one inlet channel (i.e., the vias drilled at "Inject" and "Dilute"; FIG. 1, **b**);

at least one micromixing block (i.e., at the intersection of the inlet channels, at the upper left corner of reactor **b**) positioned downstream from the at least one inlet channel;

an aging section (i.e., comprising the "serpentine" channel portion in reactor **b**) positioned downstream from the micromixing block; and

at least one outlet channel (i.e., in communication with the "Exit to flow cell" in reactor **b**) positioned downstream of the aging section;

wherein the at least one inlet channel, at least one micromixing block, aging section, and at least one outlet channel reside on one integrated substrate (i.e., a glass wafer sandwich).

The recitation of "at least one colloidal nanoparticle" adds no further patentable weight because the inclusion of a material or article worked upon by an apparatus does not further limit apparatus claims. In any event, Chan et al. discloses that the apparatus may be used for synthesizing nanoparticles (e.g., CdSe nanocrystals).

Chan et al. further discloses that the width and depth of the aging channel are within the recited ranges (i.e., a width of 200 μm and a depth of 57 μm; see description of FIG. 1). Also, the length of the aging channel (i.e., at 105 cm) meets the claim limitation of "about 100 cm". Chan et al., however, does not specify the width and depth measurement for the at least one inlet channel or the channel of the micromixing block. In any event, it would have been obvious for

one of ordinary skill in the art at the time the invention was made to select an appropriate width and depth (such as a width and depth within the instantly claimed ranges) for the various channels in the apparatus of Chan et al., on the basis of suitability for the intended use and absent showing any unexpected results thereof, because it has been held that changes in size involve only ordinary skill in the art. *In re Rose*, 220 F.2d 459, 463, 105 USPQ 237, 240 (CCPA 1955), and where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art, *In re Aller, 105 USPQ 233.*

In addition, Chan et al. is silent as to the apparatus comprising an ultrasonication means. Yasuda et al. teaches an apparatus comprising a microchannel **20**, wherein the apparatus further comprises an ultrasonication means for mixing, in the form of an ultrasonication transducer attached to the apparatus (i.e., elements **31**, **32**, **33**, **41**, **42**, **43**; see FIG. 1, 2; column 1, line 5 to column 3, line 36). It would have been obvious for one of ordinary skill in the art at the time the invention was made to provide an ultrasonication means in the apparatus of Chan et al., on the basis of suitability for the intended use and absent a showing of unexpected results thereof, because the ultrasonication means comprises a stirrer having a structure that does not cause an increase in flow resistance in the microchannel, and is not susceptible to drops remaining in the microchannel, as taught by Yasuda et al. (column 1, lines 50-54).

Regarding claims 11 and 12, Chan et al. further discloses that the apparatus comprises means for introducing a first reactant and a second reactant into a first inlet channel and a second inlet channel, respectively (i.e., via the drilled vias, labeled "Inject" and "Dilute", using syringe pumping). As defined in Applicant's specification, the means for introducing a reactant comprises an inlet port (e.g., at **14, 18, 20**; FIG. 1A; page 12, lines 23-24).

Regarding claims 13 and 118, Chan et al. further discloses that the apparatus comprises means for introducing a third reactant into a third inlet channel (i.e., via another "Dilute" via, located downstream of the serpentine channel; using syringe pumping; see FIG. 1, **b**). The recitation of a particular flow rate for the third reactant, however, adds no further patentable weight to the apparatus claim, because the flow rate is considered a process limitation.

Regarding claim 14, the modified apparatus of Chan et al. structurally meets the claims, because the particular number of reactants to be fed to a single inlet channel is considered a process or intended use limitation that adds no further patentable weight to the apparatus claim. Each inlet channel is structurally capable of conveying more than one reactant.

Regarding claims 16-18 and 117, the modified apparatus of Chan et al. structurally meets the claims because the first and second reactant streams are not considered elements of the apparatus, and their respective flow rates are considered process limitations.

Regarding claims 19-30, the modified apparatus of Chan et al. structurally meets the claims because the synthesized colloidal nanoparticles are not elements of the apparatus.

Regarding claims 33-35, 37 and 119, Chan et al. discloses a quench fluid inlet port and means for introducing quench fluid into said port (i.e., at the second drilled via labeled "Dilute", in communication with a "Dilute" channel; using syringe pumping; see FIG. 1, reactor **b**) located downstream of the aging section and upstream of the outlet channel. The recitation of a particular quench fluid, however, adds no further patentable weight the claim, since the quench fluid is not considered part of the apparatus.

Regarding claim 36, Chan et al. discloses that the apparatus comprises means for introducing at least one reactant stream into the microreactor at said at least one inlet channel

(i.e., through the drilled vias for "Dilute" or "Inject" at the upper left portion of the reactor **b**; FIG. 1), wherein the quench fluid inlet port (i.e., at the other drilled via labeled "Dilute") is adapted to introduce a quench fluid into the microreactor. The apparatus of Chan et al. structurally meets the claims because the particular flow rate of the quench fluid relative to the flow rate of the at least one reactant stream is considered a process limitation that does not further limit the apparatus.

7. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chan et al. (*Nano Letters*, 2003, Vol. 3, No. 2, pp. 199-201) in view of Yasuda et al. (US 6,244,738), as applied to claim 116 above, and further in view of Chandler et al. (US 6,506,584).

The collective teaching of Chan et al. and Yasuda et al. is silent as to whether the ultrasonication means may comprise an ultrasonication bath, in which the microreactor or a portion thereof is emersed. Chandler et al. (column 5, lines 4-26; column 7, line 24 to column 8, line 18; FIGs. 2, 4) teaches a conventionally known ultrasonication means comprising an ultrasonication transducer or an ultrasonication bath. It would have been obvious for one of ordinary skill in the art at the time the invention was made to substitute the ultrasonication means of Chandler et al. for the ultrasonication means in the modified apparatus of Chan et al., on the basis of suitability for the intended use thereof and absent showing any unexpected results thereof, because the substitution of known equivalent structures involves only ordinary skill in the art. *In re Fout* 213 USPQ 532 (CCPA 1982); *In re Susi* 169 USPQ 423 (CCPA 1971); *In re Siebentritt* 152 USPQ 618 (CCPA 1967); *In re Ruff* 118 USPQ 343 (CCPA 1958).

Response to Arguments

8. Applicant's arguments filed October 12, 2007 have been fully considered but they are not persuasive. Applicant (beginning in the last paragraph on page 7) argues,

> "... the present invention relates generally to microfluidic chemical systems for synthesis and coating of colloidal nanoparticles. The structure and dimensions of the microfluidic system is designed to ensure that flow of reactants through the device maximizes the devices ability to synthesize and coat of the nanoparticles. For example, the inlet channel and micromixing block channel dimensions as claimed control the appropriate amount and rate of reactant flowing through the device, to maximize the devices ability to coat (or grow an additional layer on) the nanoparticles. Neither Wang nor Chan disclose, teach or suggest coating of nanoparticles, and therefore, cannot suggest appropriate dimensions for the same. Applicant therefore submits that the present claims as amended are not anticipated or obviated by the references cited by the Examiner, and respectfully requests that these rejections be withdrawn."

The Examiner respectfully disagrees.

Firstly, Applicant argues that, "Neither Wang nor Chan disclose, teach or suggest *coating* of nanoparticles." However, please note that the elected claims are drawn to the "microreactor", i.e., the apparatus used for synthesizing (but not coating) the nanoparticles.

The claims directed towards the "electrophoretic switch", i.e., the apparatus that is actually used for coating the nanoparticles (see specification, page 3, line 26, to page 4, line 19), were withdrawn from consideration as being directed to a non-elected invention (see restriction requirement mailed on September 27, 2005 and Applicant's election on October 28, 2005).

Secondly, the Examiner maintains that it would have been well within the skill level of one of ordinary skill in the art to select the appropriate width and depth (such as a width and depth within the instantly claimed ranges) for the at least one inlet channel and the at least one

channel of the micromixing block in either the apparatus of Wang et al. or Chan et al., on the basis of suitability for the intended use and absent showing any unexpected results thereof, because changes in size involve only ordinary skill in the art, *In re Rose*, 220 F.2d 459, 463, 105 USPQ 237, 240 (CCPA 1955), and where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art, *In re Aller,* 105 USPQ 233.

Chow et al. (US 2002/0019059) and Kopf-Sill et al. (US 5,842,787) are cited to further support the Examiner's position. Please note that the citations of Chow et al. and Kopf-Sill et al. do not constitute a new rejection, as they are merely provided to illustrate that changes in size and optimization of dimensions would have been considered well known to those having ordinary skill in the art.

Chow et al., for example, discloses a microfluidic device comprising microchannels (see dimensions under section [0026]), wherein,

> [0057] … either time or volume controlled reagent additions to a particular region of the microfluidic device, e.g., the reaction zone, are carried out by configuring the reagent delivery channels to affect such controlled delivery. <u>In particular, the rate at which material flows through a particular microfluidic channel is defined by a number of factors, including the force applied to drive the material through the channel, the flow resistance of the channel, and the distance that material must travel through the channel. The latter two characteristics are typically dependent upon one or both of the length and cross-sectional dimensions of the channel through which the material is forced. By controlling at least one of these channel characteristics, one can effectively control the time required for the material to move through the channel and/or the volumetric rate at which material flows through that channel.</u> For example, where the connecting channel between a first reagent source and the reaction zone is shorter than the connecting

channel between the second reagent source and the reaction zone, under the same pressure level, the first reagent will reach the reaction zone first just by virtue of the longer distance that the second reagent must travel. In addition, the longer channel will have a greater level of flow resistance, further slowing the second reagent relative to the first. (emphasis added).

[0058] Similarly, where the connecting channels are the same length, but the second channel has a significantly smaller cross-sectional area, again, it will take the second reagent longer to reach the reaction channel than the first reagent. Further, the rate at which the second reagent flows into the reaction channel will also be reduced. Additionally, the differential pressure-based flow of fluids in two channels having different cross-sectional areas is further amplified in those channels having an aspect ratio (width:depth) that is greater than about 5, where one is varying the narrower dimension, e.g., depth, between the two channels. In particular, in these situations, the pressure-based volumetric flow rate of fluids is reduced by the cube of the reduction in channel depth, while the linear velocity of fluid through the channel is reduced by the square of that reduction. For example, in a pressure based system, where the second channel is one tenth as deep as the first channel, the volumetric flow in that second channel will be reduced 1000 fold over the first channel under the same applied pressure. As a result, one can vary the amount of material transported through a channel (volumetric flow) as well as the amount of time required for fluid to traverse a channel (linear velocity) by varying the channel's depth. (emphasis added).

Kopf-Sill et al., for example, also discloses a microfluidic device comprising microchannels (see dimensions at column 2, line 58 to column 3, line 18), wherein,

"The present invention, addresses this problem of microfluidic systems by providing deeper channel regions within the system, to permit adequate diffusional mixing within a shorter channel length. In particular, it takes longer for a given volume of material to travel through a deeper channel, assuming the same volume flow rate. This provides more time for materials to mix. In addition, and perhaps more importantly, the

diffusion characteristics within these deeper channels are substantially enhanced. This is evident whether one introduces two or more volumes of material, serially, or in parallel into the mixing channel. Specifically, because diffusional mixing of two adjacent material regions, e.g. in a channel, is largely dictated by lateral diffusion of the material between two material regions, by providing those regions as thinner layers, either in a serial or parallel orientation, one can substantially enhance the rate at which the two layers will substantially completely diffuse together." (column 13, lines 15-33; emphasis added). .

"By providing deeper and narrower mixing channels, one enhances the diffusional mixing of materials, without increasing the amount of hydrodynamic flow relative to the electroosmotic flow, or altering the level of electrical resistance through that channel. In particular, the area along which the adjacent material regions interface in the mixing channel is substantially increased relative to the thickness of each region. This permits the more efficient intermixing, as described. However, by maintaining at least one thin dimension within the mixing channel (typically width), or within all other channels of the microfluidic device, there is little or no increase in hydrodynamic flow effects within these channels. Alternatively, mixing channels can be narrowed to provide enhanced mixing kinetics from materials being transported in on either side of the channel. In such instances, providing these mixing channels as deeper channel portions permits such narrowing, without increasing the level of resistance across the length of that mixing channel portion." (column 13, line 50 to column 14, line 2; emphasis added).

"The dimensions of the mixing channel will typically vary depending upon the nature of the materials to be mixed. Specifically, larger molecules are slower to diffuse, and thus require a mixing channel that has either a greater length, or a greater cross-sectional area, such that the materials are substantially mixed while they are within the mixing channel. Typically, the dimensions of a mixing channel will fall within the range of dimensions for the microscale channels, described above. However, such channels will typically have an aspect ratio of less than 1, and preferably, less than or equal to 0.5, e.g., more than twice as deep as wide, more preferably, less than or equal to about 0.3, still

> more preferably, less than or equal to about 0.25, or less than or equal to about 0.2, and often in the range of about 0.1 to 0.05. In preferred instances, these mixing channel portions will have dimensions in the range of from about 2 to about 50 μm wide, while being from about 10 to about 200 μm deep. In particularly referred aspects, the mixing channels will be from about 5 to about 20 μm wide, and from about 50 to about 200 μm deep. While mixing channels can incorporate wide regions as opposed to deep regions, such wider regions occupy greater amounts of substrate area, and as such, are less preferred. In any event, mixing channel portions will typically range from about 0.1 to about 10 μm in length, and are preferably in the range of from about 0.1 to about 3 mm in length." (column 15, lines 10-39; emphasis added).

Accordingly, one having ordinary skill in the art would have known to select the appropriate width and depth for each of the at least one inlet channel and the at least one channel of the micromixing block in the apparatus of Wang et al. or Chan et al., for the intended use of achieving an optimal reactant flow rate from the at least one inlet channel to the point of reaction, as well as an optimal degree of diffusional mixing of the reactants within the at least one channel of the micromixing block, for producing nanoparticles of the desired physical characteristics, e.g., particle size.

Conclusion

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

* * *

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer A. Leung whose telephone number is (571) 272-1449. The examiner can normally be reached on 9:30 am - 5:30 pm Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Glenn A. Caldarola can be reached on (571) 272-1444. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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